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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,595	02/03/2004	Ashley Stuart Davis		1135

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/771,595	DAVIS ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 May 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a)☐ will not be entered, or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached sheets.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Advisory Action

Applicants have raised the possibility that the finality of the previous Office action (mailed 8/14/06) was premature. In support of this assertion, applicants have argued that all they did in proceeding from the claims of 12/27/05 to the claims of 5/22/06 was to incorporate the limitations of claim 7 into claim 6. However, this assertion is not in accord with the facts. While it is true that a limitation was introduced into claim 6, it is also true that the scope of claim 6 was substantially broadened in another respect. Pursuant to the amendment of 12/27/05, claim 6 was drawn to a process for stabilizing a pyrene actin composition. But in the amendment of 5/22/06, claim 6 was drawn to a method of achieving any objective, so long as the composition was concentrated and combined with a few other ingredients. Thus, while there may be some overlap between previous claim 6 (according to the amendment of 12/27/05) and the current version (amendment of 5/22/06), there are numerous embodiments which are now encompassed which were not previously. Accordingly, the finality of the previous Office action is fully justified.

Claims 1-6 & 8-22 remain pending.

✦

Claims 1-6 & 8-22 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The claims are indefinite as to the ultimate objective of the method. The claims recite only process steps, and as such, virtually any objective would be encompassed. In reponse, applicants have merely asserted that an artisan of ordinary skill could determine where the line is drawn between what is encompassed and what is not. However, applicants themselves have thus far been unwilling to explain, or speculate as to where that line might be drawn. It is not apparent, for example, what might be excluded from claim 6.

- In claim 9, the phrase "frozen second pyrene actin composition" lacks literal antecedent basis. This rejection could be readily overcome by adding the following phrase to the end of claim 8:

  thereby generating a frozen second pyrene actin composition.

  In response, applicants have argued that claim 9 is not unclear, because the composition in question is inherent. Perhaps the skilled artisan could guess what applicants intend. However, this does not mean that the claim is clear.

- In claim 12, the phrase "second pyrene actin composition" is used. As applicants have argued, the skilled artisan, upon encountering this phrase, would automatically insert the term "frozen" in front of it. Accordingly, claim 12 is calling for freezing a composition that is already frozen.

- In claim 14, the phrase "frozen second pyrene actin composition" lacks literal antecedent basis. Applicants have argued that literal antecedent basis is present. This assertion is clearly false. Moreover, in pointing to claim 12, applicants have argued that the term "frozen" should not be implied in this case. Thus, in addition to the absence of literal antecedent basis, there are inconsistencies as to when the term "frozen" is supposed to be implied, and when it is not.

✦

Claims 6, 10, 11, 15-19 are rejected under 35 U.S.C. §103 as being unpatentable over Drenckhahn (*J. Biol. Chem.* **261**, 12754, 1986) in view of Pollard T. D. (*J Cell Biol* **99**(3), 769-77, 1984)

The teachings of Drenckhahn are indicated above. The Pollard reference is cited because Drenckhahn refers to it (page 12755, col 1, paragraph 1) as the process which was used to make the pyrene actin. In addition, Pollard discloses (p. 771, col 1) a procedure in which the pyrene actin is "pelleted"; this pelleting is a form of "concentration".

In response to the foregoing, applicants have argued that Drenckhahn taken together with Pollard discloses the following sequence:

a) preparation of pyrene actin;

b) pelleting the pyrene actin;

c) depolymerizing the pyrene actin;

d) purifying the pyrene actin by chromatography on a G-150 column; and

e) mixing the pyrene actin with unlabeled actin.

Applicants have argued in effect that because Pollard does not disclose a concentration step subsequent to the chromatography on a G-150 column, it must not only be true that Pollard did not concentrate the pyrene actin (subsequent to chromatography) but that a protein chemist using the Pollard procedure would

have been dissuaded from doing so as well. Applicants' logic is unconvincing on its face. One could also point out that Pollard did not disclose that he ate lunch at any time during the procedures, and that Pollard did not disclose that he had a conversation with another person at any time during the procedure. However, it does not follow therefrom that a protein chemist following the Pollard procedure would have been persuaded that eating lunch or communicating with other humans would have somehow been undesirable. The question is whether or not motivation would have existed, or reasonably could have existed for reducing the volume of solution subsequent to the chromatography step. As a general proposition, if a protein chemist chromatographs a protein for subsequent use in a process, one of the following is generally true subsequent to the chromatography: (a) the protein solution is too concentrated, or (b) the protein solution is too dilute. Perhaps the subsequent process is an assay for growth of cells in a Petri dish. Or perhaps the protein is to be administered to an animal subject. Or perhaps the protein is going to be sequenced or otherwise analyzed. Or perhaps the protein is going to be treated with an enzyme. Or perhaps the subsequent process is a fluorescence assay. Whatever the intended process, it is generally the case that the concentration of that protein must be adjusted upward or downward to optimize the process. More often than not, chromatography of proteins results in a solution which is too dilute for subsequent use. As applicants may be aware, the basic principle in chromatography is selective

adsorption to the chromatographic matrix. If one has a multitude of products in a mixture, the objective is for the "target" protein to migrate at a different rate than the undesired components. Effective separation involves a gradual process of elution, and often large volumes of buffer are required. In general, the more difficult the separation, the larger the volumes of buffer that are required. Thus, in general, following a chromatographic purification, the "target" protein is present in a very dilute solution.

As to what exactly is the minimal concentration of actin that one could use to determine the elongation rate in sucrose is not entirely clear from a reading of the Drenckhahn reference. The likelihood, however, is that the dilute solution resulting from chromatography on the G-150 column would not be suitable for the assay. In order for the obviousness rejection to be proper, there need not be absolute, iron clad certainty as to the optimum concentration of the pyrene actin for the assay. What matters is that motivation could exist, in certain circumstances, for (at least a) partial concentration of the pyrene actin. One point to note in this regard is that, once in possession of a concentrated solution, it is a very trivial matter to dilute that solution. But to go in the other direction (i.e., concentrating the solution) is much more cumbersome and time-consuming. Thus, for the practitioner of the Drenckhahn procedure, it would make much more sense to begin with a solution of pyrene actin that is more concentrated than what may be needed, and then to effect dilutions as needed

throughout the course of the assays. This allows for rigorous control of the various concentrations with a minimum of effort. Perhaps applicants would argue that if the chromatographic procedure produced pyrene actin at a concentration of 10 nMole/liter, this would not impose any inconvenience on the practitioner of the Drenckhahn procedure. But a concentration which is perhaps 500-fold higher would indeed be more convenient and would simplify matters. Note also that Drenckhahn also conducted experiments on polymerization versus concentration of actin (see figure 4 of the reference). Having argued (in effect) that an omission of a given procedure in a reference amounts to a "teaching away" from that procedure, applicants would be in a difficult position to now argue that a practitioner would have been motivated to abstain from conducting experiments such as those in figure 4 (of the reference). In order to conduct these experiments, some concentration would be required.

In addition to the foregoing, there is another, simpler, motivation for concentrating protein solutions following a chromatographic purification. And that is simply to reduce the volume of solution for storage purposes. In many small laboratories, there are 5-10 employees for each refrigerator. Clearly, it is not possible for everyone to store all of their diluted solutions in that one refrigerator. If a given protein is present at a concentration of, e.g., 100 nMole/liter following purification, the (refrigerator) space limitations in many

laboratories require that the volume of such a solution be substantially reduced prior to storage.

Thus, although there is no specific directive (in Drenckhahn or Pollard) to reduce the volume of the pyrene actin solution, motivation exists for doing so.

The rejection is maintained.

✧

Claims 6, 10, 11, 15-19 are rejected under 35 U.S.C. §103 as being unpatentable over Drenckhahn (*J. Biol. Chem.* **261**, 12754, 1986) in view of Cooper J.A. (*Journal of muscle research and cell motility* 4(2) 253-62, 1983)

The teachings of Drenckhahn are indicated above. The Cooper reference is cited because Drenckhahn refers to Pollard (page 12755, col 1, paragraph 1) as the process which was used to make the pyrene actin; Pollard, in turn, refers to Cooper.

Applicants have argued that there is no motivation to combine references. However, this is not true. Drenckhahn provides a teaching to use the process of Pollard. Pollard, in turn, provides a teaching to use the procedure of Cooper. Thus, there is no question as to the motivation to combine references.

The issue, as above is whether a process step which is omitted from a reference amounts to a "teaching away" from that process step. As discussed above, there is motivation to use, or at least to store (under refrigeration) a partially concentrated solution of the pyrene actin, rather than a highly dilute solution.

The fact that Cooper does not discuss simple rudimentary concepts that are well known to protein chemists (not to mention aspiring protein chemists with little experience) does not mean that such concepts are unobvious.

The rejection is maintained.

✦

Claims 6, 10, 11, 15-19 are rejected under 35 U.S.C. §103 as being unpatentable over Drenckhahn (*J. Biol. Chem.* **261**, 12754, 1986).

As indicated previously, Drenckhahn discloses methods of using pyrene-actin to study rates of elongation of pyrene-labelled filaments. Also disclosed (e.g., page 12755, col 1, paragraph 2) is that sucrose inhibit elongation of actin filaments. Drenckhahn does not explicitly teach a step of concentrating the pyrene actin composition after it is prepared. However, the process of preparing the pyrene actin would result in a dilute solution of the target material; one of ordinary skill would have been motivated to increase the concentration of the pyrene actin to a point where only small volumes of the solution would be required for the subsequent assay. Further, it is more convenient to store a small volume of a concentrated solution than to store a large volume of a dilute solution.

The examiner's arguments presented above (Drenckhahn in view of Cooper) apply here as well; the rejection is maintained.

✦

Claims 6, 10, 11, 15-19 are rejected under 35 U.S.C. §103 as being unpatentable over Drenckhahn (*J. Biol. Chem.* **261**, 12754, 1986) in view of Blatt, William F. (*American Laboratory (Shelton, CT, United States)* 21-30, 1969) or Cordle (USP 4897465).

The teachings of Drenckhahn are indicated above. Drenckhahn does not explicitly teach that when one is in possession of a dilute pyrene actin composition, benefit may accrue to the practitioner upon concentrating the composition. The secondary references disclose methods of concentrating protein-containing mixtures using ultrafiltration.

One of ordinary skill would have been motivated to increase the concentration of a dilute solution of pyrene actin; the secondary references provide a means of accomplishing this.

In response applicants have asserted that Drenckhahn discloses both of the following:

(a) following chromatography, the dilute pyrene actin-containing solution should not be concentrated even partially, and

(b) following chromatography, the dilute pyrene actin-containing solution should be diluted further.

However, it is not apparent where either of these statements can be found in the reference, and applicants have not attempted to identify a location.

As noted above, applicants position is that an omission of a procedure (in a reference) is tantamount to a "teaching away" from that procedure. However, this is not the case. As noted above, there is motivation for at least a partial concentration of the pyrene-actin prior to use.

The rejection is maintained.

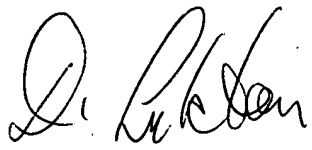
✦

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



DAVID LUKTON, PH.D.
PRIMARY EXAMINER